

Metabolomics in vivo: A tool to detect systemic toxicity in preclinical/ toxicological studies

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BASF has developed a rat plasma metabolomics data base (MetaMap[™]Tox) containing the metabolome of more than 500 data rich chemicals, agrochemicals and drugs derived from 28 day repeated dose toxicity studies in rats (adapted to the OECD 407 test guideline). Based on metabolic profiling after 7, 14 and 28 days of treatment with data rich test substances, more than 100 patterns of metabolite changes have been developed that are specific for a given toxicological effect.

Systemic toxicity of new compounds is assessed using the MetaMap[™]Tox data base routinely within BASF's experimental toxicology department. The assessment is based on the metabolite changes observed, the comparison of the metabolome of the test compound against the specific toxicity patterns with MetaMap[®]Tox and a correlation analysis of the whole test compound metabolome against the whole metabolomes of all reference compounds in the data base. The metabolomics approach used by BASF SE delivers valuable additional results which are used for decision making in terms of follow-up investigations, selection of best candidates and as additional mechanistic information for hazard assessment. In order to show the applicability of MetaMap[™]Tox for preclinical studies, case studies will be presented on the systemic toxicity of cyclosporine A, phenytoin, and amiodarone.